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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/013,071	12/10/2001	Zhaoning Zhu	IN01174	1388

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PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER	
MONDESI, ROBERT B	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/013,071	ZHU ET AL.	
	Examiner	Art Unit	
	Robert B Mondesi	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18 and 21-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18, 21-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to amendment filed June 30, 2004. **Claims 19-20 and 24-94** are cancelled. **Claims 1-18 and 21-23** are currently pending.

Priority

The current application filed on December 01, 2001 claims priority to provisional application 60/254,869 filed on December 12, 2000.

Withdrawal of Objections and Rejections

The rejection of **claims 19 and 22** under 35 U.S.C § 112, second paragraph is withdrawn.

The provisional rejection of **claims 1 and 19-23** under the judicial doctrine of obviousness type double patenting as being unpatentable over claim 1 of copending Application No. 09/825,399 is withdrawn.

Maintenance of rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-18 and 21-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for macrocyclic compounds 26 and 27 in table A (pages 113) and in the specification examples 19-23 (pages 92-105), does not reasonably provide enablement for all the compounds presented by the general

structure formula (I) of claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use or make the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir.1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the relative skill of those in the art, (5) the predictability or unpredictability of the art, (6) the amount or direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary. Although the quantity of experimentation alone is not dispositive in a determination of whether the required experimentation is undue, this factor does play a central role. For example, a very limited quantity of experimentation may be undue in a fledgling art that is unpredictable where no guidance or working examples are provided in the specification and prior art, whereas

the same amount of experimentation may not be undue when viewed in light of some guidance or a working example or the experimentation required is in a predictable established art. Conversely, a large quantity of experimentation would require a correspondingly greater quantum of guidance, predictability and skill in the art to overcome classification as undue experimentation. In Wands, the determination that undue experimentation was not required to make the claimed invention was based primarily on the nature of the art, and the probability that the required experimentation would result in successfully obtaining the claimed invention. (Wands, 8 USPQ2d 1406). Thus, a combination of factors which, when viewed together, would provide an artisan of ordinary skill in the art with an expectation of successfully obtaining the claimed invention with additional experimentation would preclude the classification of that experimentation as undue. A combination of Wands factors, which provide a very low likelihood of successfully obtaining the claimed invention with additional experimentation, however, would render the additional experimentation undue.

1.Breadth of the claims.

In regards to the product of the invention and the breadth of the claims the broadest interpretation that applies is to compounds presented by the general structure formula (I) of claim 1.

2. The nature of the invention.

The invention is a novel class of pharmaceutical compounds that are inhibitors of Hepatitis C Virus (HCV) protease activity, specifically macrocyclic compounds that inhibit HCV NS3/NS4a serine protease activity.

3. The state of prior art.

In regards to the macrocyclic compounds of the invention presented by the general structure formula (I) of claim 1, the prior art does not provide any evidence of HCV protease inhibitory activity- specifically with regards to HCV NS3/NS4a serine protease inhibitory activity.

4. The relative skill in the art.

The relative skill in the art as it relates to pharmaceutical macrocyclic compounds that inhibit the activity of HCV serine protease is that of a M.D. or Ph. D. level individual.

5. The level of predictability in the art.

Since the prior art does not teach that the compounds presented by general formula (I) of claim 1 formerly existed, the level of predictability is low in regards to the macroclycic compounds of the invention with respect to HCV serine protease inhibitory activity. Therefore, one of skill in the art would not be able to readily anticipate the inhibitory effects of the macrocyclic compounds of the invention in view of HCV NS3/NS4a serine protease inhibitory activity.

6. The amount of guidance present.

The applicant has not provided guidance for all the compounds presented in the general formula (I) of claim 1. In table A of the specification of the present application , the applicant has provided results of a HCV protease continuous assay for a group of macrocyclic compounds wherein the applicant has categorized the Ki values associated with each investigated compound as a barometer of HCV serine protease inhibitory activity. If the Ki of a given compound is between 1-99nM then the compound is in

category a, any value for a given compound that is above 100nM and below 999nM is considered to be in category b, if the Ki value is between 1000-9999nM the compound is considered to be in category c and if the Ki value is between 10,000-50,000 then the compound is considered to be in category d. The applicant has shown some guidance as to how certain macrocylic compounds of the invention (table A, compounds 26 and 27, page 113) can be used to perhaps inhibit HCV protease activity - but the applicant has not provided guidance for all the compounds presented in the general structure formula (I) of claim 1 in regards to how they can be used to inhibit HCV serine protease activity.

7. The existence of working examples.

The specification, examples 19-23 (pages 92-105) provides specific working examples of macrocyclic compounds (table 1) that can be used to inhibit HCV serine protease activity. However, the specification does not provide working examples of all compounds suggested by the general structure formula (I) of claim 1.

8. The quantity of experimentation necessary.

In the case of using all the compounds suggested by the general structure formula (I) of claim 1, a large quantity of experimentation needs to be disclosed in order for a person skill in the art to be able to practice the invention, since there are a multitude of possible compounds that are suggested by the general structure formula of claim 1 and each compound needs to be tested for HCV protease inhibitory activity.

Due to the quantity of experimentation still required to be performed by one skill in the art in regards to how to use all the compounds suggested by

the general formula (I) of claim 1, the lack of guidance presented in the specification regarding the same, the absence of a working example directed to same, the unpredictable nature of the invention with regards to HCV serine protease inhibitory activity, the state of the prior art not providing any evidence that all the compounds suggested by general formula (I) of claim 1 will exhibit HCV serine protease inhibitory activity , and the breath of the claims which fails to provide particular steps for all compounds suggested by the general formula (I) of claim 1 exhibiting HCV serine protease inhibitory activity, the specification fails to teach the skilled artisan in the art how to make and use the invention.

Response to applicant's arguments

Applicants assert and submit on the record that only a number of compounds, by activity data, experimentation and individual structures have been disclosed. Applicants further cite the following case law; *Atlas Powder Co. V. E.I Dupont De Nemours Co.* 750 F-2d 1569.,1576, 224 U.S.P.Q. (BNA) 409, 413 (Fed. Cir. 1984)., *Amgen, Inc. v. Chugai Pharmaceutical Co., LTD.,,* 18 U.S.P.Q2d (BNA) 1016, 1027 (Fed, Cir 1991) and assert further that the vast amount of details , compounds, variety of molecules and particulars that are provided in the present case are sufficient enough to fully satisfy the enablement requirement.

In response to the applicants assertions the examiner would like to point out that the mentioned case law merely restate the enablement requirement that the rejection is based on and do not provide any further arguments to support the applicants assertion

that the rejection of claims 1-18, 21-23 should be withdrawn. Furthermore the examiner would like to state that the reason for the rejection is that the scope of the compound general structure formula in claim 1 has not been sufficiently supported by the present application in order to meet the enablement requirement under §112 first paragraph. The amount of details, experimentation, activity and particulars that are provided in the present case are sufficient enough to only satisfy the enablement requirement with regards to the disclosed macrocyclic compounds in table A (compounds 26 and 27, page 113) the specification, examples 19-23 (pages 92-105) and not all the compounds represented by the general structure formula of claim 1.

Conclusion

No claims are allowed

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert B Mondesi whose telephone number is 571-272-0956. The examiner can normally be reached on 9am-5pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert B. Mondesi
Patent Examiner
Group 1653
09-09-04

ROBERT A. WAX
PRIMARY EXAMINER